

WHAT IS CLAIMED IS:

1. A Chinese hamster ovary tissue-derived CHO cell into which a gene encoding an antibody molecule is introduced, which produces an antibody composition comprising an antibody molecule having complex *N*-glycoside-linked sugar chains bound to the Fc region, wherein among the total complex *N*-glycoside-linked sugar chains bound to the Fc region in the composition, the ratio of a sugar chain in which fucose is not bound to *N*-acetylglucosamine in the reducing end in the sugar chain is 20% or more.

sub a' 2. The CHO cell according to claim 1, wherein the sugar chain to which fucose is not bound is a complex *N*-glycoside-linked sugar chain in which 1-position of fucose is not bound to 6-position of *N*-acetylglucosamine in the reducing end through α -bond.

3. The CHO cell according to claim 1 or 2, wherein the antibody molecule belongs to an IgG class.

4. The CHO cell according to any one of claims 1 to 3, wherein the activity of an enzyme relating to the synthesis of an intracellular sugar nucleotide, GDP-fucose and/or the activity of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through α -bond in the complex *N*-glycoside-linked sugar chain is decreased or deleted.

5. The CHO cell according to claim 4, wherein the enzyme relating to the synthesis of an intracellular sugar nucleotide, GDP-fucose is an enzyme selected from the group consisting of the following (a), (b) and (c):

(a) GMD (GDP-mannose 4,6-dehydratase);

(b) Fx (GDP-keto-6-deoxymannose 3,5-epimerase, 4-reductase);

(c) GFPP (GDP-beta-L-fucose pyrophosphorylase).

6. The CHO cell according to claim 5, wherein the GMD is a protein encoded by a DNA of the following (a) or (b):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:65;

(b) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:65 under stringent conditions and encodes a protein having GMD activity.

7. The CHO cell according to claim 5, wherein the GMD is a protein selected from the group consisting of the following (a), (b) and (c):

(a) a protein comprising the amino acid sequence represented by SEQ ID NO:71;

(b) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:71 and has GMD activity;

(c) a protein which comprises an amino acid sequence having a homology of at least 80% with the amino acid sequence represented by SEQ ID NO:71 and has GMD activity.

8. The CHO cell according to claim 5, wherein the Fx is a protein encoded by a DNA of the following (a) or (b):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:48;

(b) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:48 under

stringent conditions and encodes a protein having GFPP activity.

30. The cell according to claim 24, wherein the GFPP is a protein selected from the group consisting of the following (a), (b) and (c):

(a) a protein comprising the amino acid sequence represented by SEQ ID NO:73;

(b) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:73 and has GFPP activity;

(c) a protein which comprises an amino acid sequence having a homology of at least 80% with the amino acid sequence represented by SEQ ID NO:73 and has GFPP activity.

Sub 26 31. The cell according to claim 23, wherein the enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in the N-glycoside-linked sugar chain is α -1,6-fucosyltransferase.

32. The cell according to claim 31, wherein the α -1,6-fucosyltransferase is a protein encoded by a DNA selected from the group consisting of the following (a), (b), (c) and (d):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:1;

(b) a DNA comprising the nucleotide sequence represented by SEQ ID NO:2;

(c) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:1 under

stringent conditions and encodes a protein having α -1,6-fucosyltransferase activity,;

(d) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:2 under stringent conditions and encodes a protein having α -1,6-fucosyltransferase activity.

33. The cell according to claim 31, wherein the α -1,6-fucosyltransferase is a protein selected from the group consisting of the following (a), (b), (c), (d), (e) and (f):

(a) a protein comprising the amino acid sequence represented by SEQ ID NO:23;

(b) a protein comprising the amino acid sequence represented by SEQ ID NO:24;

(c) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:23 and has α -1,6-fucosyltransferase activity;

(d) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:24 and has α -1,6-fucosyltransferase activity;

(e) a protein which comprises an amino acid sequence having a homology of at least 80% with the amino acid sequence represented by SEQ ID NO:23 and has α -1,6-fucosyltransferase activity;

(f) a protein which comprises an amino acid sequence having a homology of at least 80% with the amino acid sequence represented by SEQ ID NO:24 and has α -1,6-fucosyltransferase activity.

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34. The cell according to any one of claims 23 to 33, wherein the genetic engineering technique is a technique selected from the group consisting of the following (a), (b), (c) and (d):

(a) a gene disruption technique targeting a gene encoding the enzyme;

(b) a technique for introducing a dominant negative mutant of a gene encoding the enzyme;

(c) a technique for introducing mutation into the enzyme;

(d) a technique for inhibiting transcription and/or translation of a gene encoding the enzyme.

35. The cell according to any one of claims 23 to 34, which is resistant to at least a lectin which recognizes a sugar chain in which 1-position of fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through α -bond in the *N*-glycoside-linked sugar chain.

36. The cell according to any one of claims 23 to 35, which is a cell selected from the group consisting of the following (a) to (i):

(a) a CHO cell derived from a Chinese hamster ovary tissue;

(b) a rat myeloma cell line, YB2/3HL.P2.G11.16Ag.20 cell;

(c) a mouse myeloma cell line, NSO cell;

(d) a mouse myeloma cell line, SP2/0-Ag14 cell;

(e) a BHK cell derived from a syrian hamster kidney tissue;

(f) an antibody-producing hybridoma cell;

(g) a human leukemia cell line Namalwa cell;

(h) an embryonic stem cell;

(i) a fertilized egg cell.

37. The cell according to ~~any one of claims 23 to 36 into which~~ a gene encoding an antibody molecule is introduced.

38. The cell according to claim 37, wherein the antibody molecule belongs to an IgG class.

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39. A method for producing an antibody composition, which comprises culturing the ~~cell according to claim 37 or 38~~ in a medium to produce and accumulate the antibody composition in the culture; and recovering the antibody composition from the culture.

40. The method according to claim 39, which produces an antibody composition having higher antibody-dependent cell-mediated cytotoxic activity than an antibody composition obtained from its parent cell line.

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41. An antibody composition which is produced using the method according to claim 39 or 40.

42. A transgenic non-human animal or plant or the progenies thereof, comprising a genome which is modified such that the activity of an enzyme relating to the synthesis of an intracellular sugar nucleotide, GDP-fucose and/or the activity of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in the N-glycoside-linked sugar chain is decreased.

43. The transgenic non-human animal or plant or the progenies thereof according to claim 42, wherein a gene encoding the enzyme relating to the synthesis of an

stringent conditions and encodes a protein having Fx activity.

47. The transgenic non-human animal or plant or the progenies thereof according to claim 44, wherein the GFPP is a protein encoded by a DNA of the following (a) or (b):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:51;

(b) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:51 under stringent conditions and encodes a protein having GFPP activity.

Sub a¹⁰ 48. The transgenic non-human animal or plant or the progenies thereof according to claim 42 or 43, wherein the enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in the N-glycoside-linked sugar chain is α -1,6-fucosyltransferase.

49. The transgenic non-human animal or plant or the progenies thereof according to claim 48, wherein the α -1,6-fucosyltransferase is a protein encoded by a DNA selected from the group consisting of the following (a), (b), (c) and (d):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:1;

(b) a DNA comprising the nucleotide sequence represented by SEQ ID NO:2;

(c) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:1 under stringent conditions and encodes a protein having α -1,6-fucosyltransferase activity;

(d) a DNA which hybridizes with the DNA comprising the nucleotide sequence represented by SEQ ID NO:2 under stringent conditions and encodes a protein having α -1,6-fucosyltransferase activity.

Sub Q¹¹ 50. The transgenic non-human animal or plant or the progenies thereof according to any one of claims 42 to 49, wherein the transgenic non-human animal is an animal selected from the group consisting of cattle, sheep, goat, pig, horse, mouse, rat, fowl, monkey and rabbit.

51. A method for producing an antibody composition, which comprises introducing a gene encoding an antibody molecule into the transgenic non-human animal or plant or the progenies thereof according to any one of claims 42 to 50; rearing the animal or plant; isolating tissue or body fluid comprising the introduced antibody from the reared animal or plant; and recovering the antibody composition from the isolated tissue or body fluid.

52. The method according to claim 51, wherein the antibody molecule belongs to an IgG class.

Sub Q¹² 53. The method according to claim 51 or 52, which produces an antibody composition having higher antibody-dependent cell-mediated cytotoxic activity than an antibody composition obtained from a non-human animal or plant or the progenies thereof whose genome is not modified.

54. An antibody composition which is produced using the method according to any one of claims 51 to 53.

55. A medicament comprising the antibody composition according to any one of claims 21, 22, 41 and 54 as an active ingredient.

56. The medicament according to claim 55, wherein the medicament is a diagnostic drug, a preventive drug or a therapeutic drug for diseases accompanied by tumors, diseases accompanied by allergies, diseases accompanied by inflammations, autoimmune diseases, circulatory organ diseases, diseases accompanied by viral infections or diseases accompanied by bacterial infections.

57. A protein selected from the group consisting of the following (a), (b), (c), (d), (e), (f), (g), (h), (i) and (j):

(a) a protein comprising the amino acid sequence represented by SEQ ID NO:71;

(b) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:71 and has GMD activity;

(c) a protein comprising the amino acid sequence represented by SEQ ID NO:72;

(d) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:72 and has Fx activity;

(e) a protein comprising the amino acid sequence represented by SEQ ID NO:73;

(f) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:73 and has GFPP activity;

(g) a protein comprising the amino acid sequence represented by SEQ ID NO:23;

(h) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid

sequence represented by SEQ ID NO:23 and has α -1,6-fucosyltransferase activity;

(i) a protein comprising the amino acid sequence represented by SEQ ID NO:24;

(j) a protein which comprises an amino acid sequence in which at least one amino acid is deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:24 and the α -1,6-fucosyltransferase activity.

58. A DNA which encodes the protein according to claim 57.

59. A DNA selected from the group consisting of the following (a), (b), (c), (d) and (e):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:1;

(b) a DNA comprising the nucleotide sequence represented by SEQ ID NO:2;

(c) a DNA comprising the nucleotide sequence represented by SEQ ID NO:65;

(d) a DNA comprising the nucleotide sequence represented by SEQ ID NO:48;

(e) a DNA comprising the nucleotide sequence represented by SEQ ID NO:51.

60. A genome DNA selected from the group consisting of the following (a), (b) and (c):

(a) a genome DNA comprising the nucleotide sequence represented by SEQ ID NO:3;

(b) a genome DNA comprising the nucleotide sequence represented by SEQ ID NO:67;

(c) a genome DNA comprising the nucleotide sequence represented by SEQ ID NO:70.

